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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/613,903	07/11/2000	Heather J. Jordan	IVGN 187.1 CON	1446
65482 7590 03/03/2008 INVITROGEN CORPORATION C/O INTELLEVATE P.O. BOX 52050 MINNEAPOLIS, MN 55402				
EXAMINER SISSON, BRADLEY L				
ART UNIT		PAPER NUMBER		
1634				
MAIL DATE		DELIVERY MODE		
03/03/2008		PAPER		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

09/613,903

Applicant(s)

JORDAN, HEATHER J.

Examiner

Bradley L. Sisson

Art Unit

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Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 December 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 85-124, 126, 127 and 135-140 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 85-124, 126, 127 and 135-140 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
- 4) ☐ Interview Summary (PTO-413)
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____
- Paper No(s)/Mail Date _____

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 06 December 2007 has been entered.

Claim Objections

2. Claim 139 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 85, from which it depends, requires the fragments to have "substantially equal" relative mass. Claim 139 requires the relative mass to be "about the same." Such language is deemed to not further limit claim 139.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 85-124, 126, 127, and 135-140 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
5. Claims 85-124 and 139 are indefinite with respect to what constitutes the metes and bounds of "substantially equal" relative mass.
6. Claims 85-124, 126, 127, and 135-140 are confusing in terms of how the relative mass is being determined. As an initial matter, claim 85, which is exemplary of the claims, requires the "relative mass of the nucleic acid fragments of each size, measured in base pairs, is substantially equal." It is not clear from the claim, and the depending claims, if the mass is on a molecule-by-molecule basis, or whether the mass is the cumulative total for all molecules present at a given size.
7. Said claims are also not clear as to how the mass is to be measured in "base pairs" when there is no requirement that the fragments be double stranded.
8. Claims 85-124, 126, 127, and 135-140 are confusing as to how the term "fragment" and "plurality" is to be construed. For example, is the expression "plurality of fragments" to be construed as being the plurality of fragments that would go to form a single band in an electrophoretic gel, or is the expression to be construed as being directed to that which would form a number of different bands. Using claims 85 and 91 as an example, claim 85 seemingly refers to there being a plurality of "fragments" at a given size, yet claim 91 seemingly refers to a plurality of fragments that range in size. Given such dual usage of the term "plurality" and "fragments," it is less than clear how the term is to be construed in the varying applications.

9. The manner by which the relative mass is being calculated is not clear. As presently worded, the composition could have nucleic acid fragments that have any of a number of non-naturally-occurring nucleotides, and which may, or may not, have mass-modifying labels upon them. While the overall length may be one value, the mass of the fragments may well be something that does not correlate directly with typical nucleotide masses. Further, the composition could have secondary structures, which would suggest a greater mass, yet the actual mass of the fragment(s) does not correlate with the length in base pairs. An example of this situation would be non-linear DNA trying to migrate through a gel v. linear, single-stranded nucleic acid migrating through the same gel in response to the same electromotive force.

Claim Rejections - 35 USC § 102/103

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

12. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

13. Claims 85-101, 103-121, 123, 124, 126, 127, and 135-140 are rejected under 35

U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over US Patent 5,316,908 (Carlson et al.).

14. Carlson et al., Fig. 1, disclose a nucleic acid ladder that meets the size, relative mass, and intensity requirements of claims 85-101, 103-121, 123, 124, 126, 127, and 135-140.

15. It is noted that claims 85 and 105 are drawn to a nucleic acid ladder composition. The claims do not require that the ladder actually be part of any electrophoretic system or that they be stained, or even if they are stained, that the label be caused to fluoresce. Rather, the claims identify a range of fragment sizes. Acknowledgement is made of the requirement that the fragments be of "substantially equal mass," however, the metes and bounds of this expression are not clear; see rejection of claims under 35 USC 112, second paragraph, *supra*.

16. It is noted with particularity that a compound and its properties are inseparable. While one may identify new properties or new means for evaluating same, such does not make an old compound, or old composition, new and patentable.

17. The claims recite no chemical or physical component that would make the nucleic acid of the claims any different from the nucleic acid ladders of the prior art.

18. While Fig. 1 is a drawing and not a photograph, the specification does state that the Figure does represent the migration of the nucleic acid ladder in an electrophoretic environment. Said Figure clearly shows that the bands have the same relative intensity.

19. To the extent that claims 103 and 123 do positively recite that the ladder is stained with ethidium bromide, it is noted that Carlson et al. disclose such, at column 4. For purposes of examination, ethidium bromide is construed to meet the requirements of a dye as it is typically used to stain the entire gel, and with it, stain (dye) preferentially the nucleic acids therein. Accordingly, a limitation of claims 101, 103, 104, 123 and 124 are deemed to be met by the disclosure of Carlson et al.

20. Carlson et al., disclose nucleic acid ladders that comprise numerous bands that span a wide range of fragment sizes. While some of the rungs of the nucleic acid ladder fall within the recited ranges of claims 126, 127, and 135-140, the disclosed nucleic acid ladders also comprise additional nucleic acid fragments that are outside of the recited range. Such additional bands do not detract from the instant rejection as the claims, through the use of the term "comprises," allows for the inclusion of additional reagents, even in significant amounts.

21. The claims do not recite any material difference in the composition of the nucleic acid that the individual fragments are comprised of. Further, there is no specific wording as to the copy number of the fragments of any given size, or combination of sizes. And as presented above, the exact meaning of the expression "substantially equal" is indefinite, for which claims have been rejected. Accordingly, and in the absence of convincing evidence to the contrary, the prior art is deemed to anticipate the claimed invention.

22. Should the prior art not anticipate the claimed invention, the selection of which band or combination of bands, and their relationship to one another is not deemed to constitute a patentable distinction over the prior art. Rather, such limitations are deemed to be the result of design choice and/or routine optimization.

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23. It is well settled that routine optimization is not patentable, even if it results in significant improvements over the prior art. In support of this position, attention is directed to the decision in *In re Aller, Lacey, and Hall*, 105 USPQ 233 (CCPA 1955):

Normally, it is to be expected that a change in temperature, or in concentration, or in both, would be an unpatentable modification. Under some circumstances, however, changes such as these may impart patentability to a process if the particular ranges claimed produce a new and unexpected result which is different in kind and not merely in degree from the results of the prior art. In *re Dreyfus*, 22 C.C.P.A. (Patents) 830, 73 F.2d 931, 24 USPQ 52; In *re Waite et al.*, 35 C.C.P.A. (Patents) 1117, 168 F.2d 104, 77 USPQ 586. Such ranges are termed "critical" ranges, and the applicant has the burden of proving such criticality. In *re Swenson et al.*, 30 C.C.P.A. (Patents) 809, 132 F.2d 1020, 56 USPQ 372; In *re Scherl*, 33 C.C.P.A. (Patents) 1193, 156 F.2d 72, 70 USPQ 204. However, even though applicant's modification results in great improvement and utility over the prior art, it may still not be patentable if the modification was within the capabilities of one skilled in the art. In *re Sola*, 22 C.C.P.A. (Patents) 1313, 77 F.2d 627, 25 USPQ 433; In *re Normann et al.*, 32 C.C.P.A. (Patents) 1248, 150 F.2d 708, 66 USPQ 308; In *re Irmischer*, 32 C.C.P.A. (Patents) 1259, 150 F.2d 705, 66 USPQ 314. More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. In *re Swain et al.*, 33 C.C.P.A. (Patents) 1250, 156 F.2d 239, 70 USPQ 412; *Minnesota Mining and Mfg. Co. v. Coe*, 69 App. D.C. 217, 99 F.2d 986, 38 USPQ 213; *Allen et al. v. Coe*, 77 App. D. C. 324, 135 F.2d 11, 57 USPQ 136. (Emphasis added)

24. The plurality of bands that make up each rung in the ladder of *Carlson et al.*, are deemed to have "substantially relative equal mass" as the band is shown to be sharp, indicating equal migration, and of same intensity with the other bands. Accordingly, a limitation of claims 126, 127, and 135-140 is deemed to be met by the prior art of record.

Response to argument

25. At page 9 of the response of 06 December 2007, hereinafter the response, applicant asserts, *inter alia*:

Because the claims prosecuted herein require that the relative mass (claims 85-104 and 140) or the total mass (claims 105-139) of each fragment in the ladder be substantially equal, *Carlson et al.* fails to disclose all of the limitations of these claims.

26. The above argument has been fully considered and has not been found to be persuasive towards the withdrawal of the rejection. As presented above, the expression “substantially equal mass” is deemed to be indefinite.

27. At page 10, bridging to page 11 of the response, argument is presented that it would not have been obvious to one of ordinary skill in the art to have modified the number of fragment copy number as such would “lead to an increase in the relative mass or the total mass of the larger fragments.”

28. The above argument has not been found to be persuasive towards the withdrawal of the rejection, as the expression has been deemed indefinite. Further, it is noted that in accordance with claim 135, the relative mass is allowed to range by a factor of 3. Each band of the ladder of Carlson shows fragments that are clearly separated. Such a narrow band speaks to the fragments of each band being of relatively equal mass, else the individual bands would not have been so narrow. Further, the intensity of each band, relative to that of the others, is equal, which speaks to the relative masses being equal.

29. Attention is directed to the decision in *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007)

When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill in the art has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense.

30. It is further noted that prior art is not limited to the four corners of the documentary prior art being applied. Prior art includes both the specialized understanding of one of ordinary skill in the art, and the common understanding of the layman. It includes “background knowledge

possessed by a person having ordinary skill in the art. . . [A] court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ.” *KSR* at 1396.

31. Suggestion, teaching or motivation does not have to be explicit and “may be found in any number of sources, including common knowledge, the prior art as a whole or the nature of the problem itself” *Pfizer, Inc. v. Apotex, Inc.* 480 F.3d 1348, 82 USPQ2d 1321 (Fed. Cir. 2007) citing *Dystar Textilfarben GMBH v. C. H. Patrick Co.*, 464 F.3d 1356 (Fed. Cir. 2006).

32. Claims 102 and 122 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,316,908 (Carlson et al.) in view of Schneeberger et al.

33. Carlson et al., Fig. 1, disclose a nucleic acid ladder that meets the size, relative mass, and intensity requirements of claims 85-101, 103-121, 123, 124, 126, 127, and 135-140.

34. It is noted that claims 85 and 105 are drawn to a nucleic acid ladder composition. The claims do not require that the ladder actually be part of any electrophoretic system or that they be stained, or even if they are stained, that the label be caused to fluoresce. Rather, the claims identify a range of fragment sizes. Acknowledgement is made of the requirement that the fragments be of “substantially equal mass,” however, the metes and bounds of this expression are not clear; see rejection of claims under 35 USC 112, second paragraph, *supra*.

35. It is noted with particularity that a compound and its properties are inseparable. While one may identify new properties or new means for evaluating same, such does not make an old compound, or old composition, new and patentable.

36. The claims recite no chemical or physical component that would make the nucleic acid of the claims any different from the nucleic acid ladders of the prior art.

37. While Fig. 1 is a drawing and not a photograph, the specification does state that the Figure does represent the migration of the nucleic acid ladder in an electrophoretic environment. Said Figure clearly shows that the bands have the same relative intensity.

38. To the extent that claims 103 and 123 do positively recite that the ladder is stained with ethidium bromide, it is noted that Carlson et al. disclose such, at column 4. For purposes of examination, ethidium bromide is construed to meet the requirements of a dye as it is typically used to stain the entire gel, and with it, stain (dye) preferentially the nucleic acids therein. Accordingly, the disclosure of Carlson is deemed to meet a limitation of claims 101, 103, 104, 123 and 124.

39. The plurality of bands that make up each rung in the ladder of Carlson et al., are deemed to have “substantially relative equal mass” as the band is shown to be sharp, indicating equal migration, and of same intensity with the other bands. Accordingly, a limitation of claims 126, 127, and 135-140 is deemed to be met by the prior art of record.

40. Carlson et al., discloses using a dye to stain the nucleic acid ladder but does not disclose using SYBR green.

41. Schneeberger et al., page 235, disclose that in conducting PCR, the formation of heteroduplexes can be eliminated by reducing the cycles of amplification from 30 to 25, but that this typically comes with a significant loss in sensitivity. Schneeberger et al., go on to teach, “sensitivity can be restored by using a novel and extremely sensitive DNA stain,” which is SYBR Green. Schneeberger et al., page 235, right column, teach that SYBR Green is five times as sensitive as ethidium bromide.

42. In view of the teachings of the prior art, one would have been motivated to have modified the nucleic acid ladder of Carlson et al., by staining same with SYBR green as disclosed by Schneeberger et al., as such is explicitly disclosed as being extremely sensitive stain which can be used in place of ethidium bromide. As disclosed by Schneeberger et al., when conducting PCR and running the amplicons on a gel, increased sensitivity is achieved by using SYBR green, which in turns allows for fewer rounds of amplification and the artifact associated therewith.

43. In view of the detailed teachings, said ordinary artisan would have been highly motivated and would have also had a most reasonable expectation of success.

Response to argument

44. At page 10 of the response argument is presented that the rejection should be withdrawn as Carlson et al., does not anticipate the claimed invention as it does not disclose fragments that are of substantially equal relative mass or total mass.

45. As presented above, the expression “substantially equal” has not been found to be defined and as such, claims have been rejected under 35 USC 112, second paragraph. In the absence of convincing evidence to the contrary, the number of fragments that one can have at given sizes of the ladder are deemed to be taught, or alternative, obvious in view of the disclosure of Carlson et al.

Conclusion

46. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571) 272-0751. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

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47. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, Ph.D. can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

48. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Bradley L. Sisson/
Primary Examiner, Art Unit 1634